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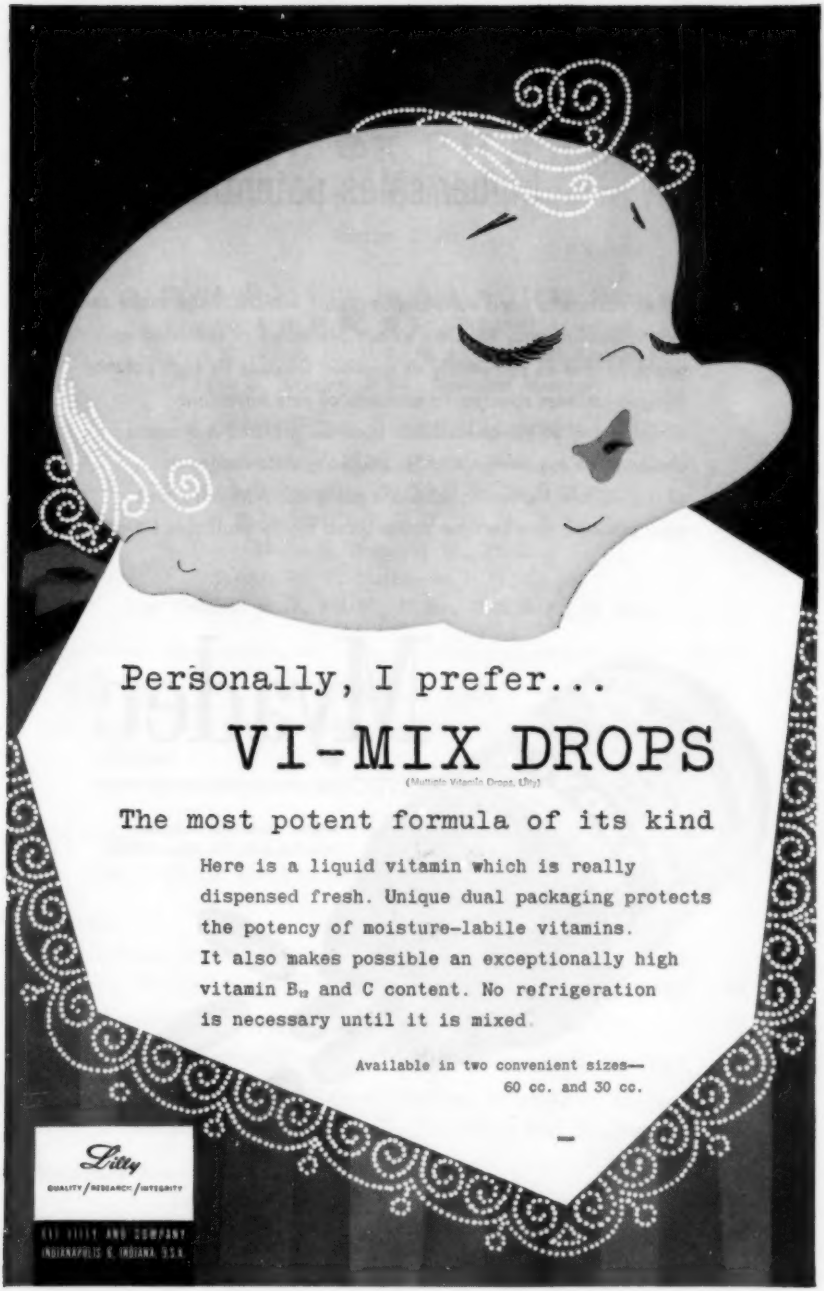
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E D I T O R I A L

THE PLIGHT OF THE PHYSICIAN IN BRITAIN

WHEN the National Health Service came into being in Britain in 1948, we did not share the enthusiasm expressed in some quarters for this program. Even the medical and pharmaceutical professions in Britain had doubts over their future under governmental control. The events of the past eight years have proved how valid these doubts and fears were, for the situation has deteriorated until the quality of medical service is, by our standards, poor indeed. Some recent developments in Britain give us evidence of the sorry plight of physicians there who are enmeshed in an unyielding bureacracy which can and does ignore their protests and disillusionment.

The financial return of the British physician, in spite of hordes of patients, is unbelievably low. If our calculations are correct, a physician attending all the medical needs of 1500 patients throughout an entire year receives the handsome sum of less than $5000. To earn this, he must make as many house calls and permit as many office visits as the *patient himself* deems necessary with no increased remuneration. The highest paid specialist in any category cannot earn over $15,000 annually, even if he has a world-wide reputation. After taxes, he is not as well off as a truck driver in the United States!

Some of this difficulty is undoubtedly caused by the overall economic plight which Britain suffers but much is due to the confidence which the Ministry of Health has that physicians will not strike as does labor. If labor were not paid with the cost of living as some index of wages, a strike would be certain. The Ministry in replying to demands of physicians that their pay keep pace with rising living costs, which it has not done, stated that "the Government owed it to the country to do everything possible to combat inflation."

If the economic evils besetting the physician were their only difficulties, it might be excusable but such is not the case. Physicians' offices are so crowded with people having trivial complaints and others seeking certification of illness as an excuse for absenteeism that there is no time for the person who is really ill. A medical Dean

in England recently wrote that "under the National Health Service doctors are progressively losing their freedom and status as a learned profession." He said further that "many physicians had given up the struggle and were resigned to treating symptoms with bottles of medicine and certificates." Time and the pressure of hundreds of patients make it necessary to either treat the really ill person empirically or bundle him off to the hospital where, if he can gain admission, he may receive proper treatment. In neither case can the physician maintain his self-respect or feel like other than a public lackey.

The ideals of an all-inclusive national health program are often looked upon by certain "starry eyed" reformers as something that could be easily attained and yet hold no threat to medical progress or the quality of medical care. While a nationalized health service does presumably offer medical care to all, it guarantees that all will get an equal privilege to share in a program of insufferable mediocrity. It, furthermore, debases the medical profession and lowers it to the level of day to day expediency. Experience in Britain should serve to crystallize the opposition to any such plan in the United States. Moreover, we should take care that a national program is not accomplished here by the adroit and tactically skillful plan of gradually covering more and more people by veterans' plans, Medicare, and all the other well-intentioned programs which eventually lead to the same end.

"Free" medical care has a powerful political appeal and the layman cannot appreciate its hazards and disadvantages. Those in the health professions must stand resolutely against this force which will engulf us forever if our solid line of defense is ever breached. Pharmacy and Medicine stand to win or lose together in the coming battle as our future like our past is inseparably entwined.

L. F. Tice

ENVIRONMENTAL DISINFECTION—A FACTOR IN THE CONTROL OF STAPHYLOCOCCAL HOSPITAL SEPSIS

By Emil G. Klarmann *

Introductory Remarks

AS IS well known, the commerce in disinfectants and related materials in the United States is regulated by a government authority —viz., the U. S. Department of Agriculture which operates under the relevant provisions of the "Federal Insecticide, Fungicide and Rodenticide Act". While the title of this statute may not appear to cover disinfectants, the law actually extends to these materials by virtue of the definition of the term "fungi", which for the purpose of this Act means "all non-chlorophyll-bearing thallophytes" including "bacteria, except those on or in living man or other animals". For the sake of completeness, it should be added that a disinfectant may fall also within the purview of another statute—viz., the "Federal Food, Drug and Cosmetic Act", which is enforced by the Food and Drug Administration of the U. S. Department of Health, Education and Welfare. The latter law may apply here in view of the definition of the term "drug" which, among other things, means "articles intended for use in the . . . prevention of disease in man or other animals". The following notes are concerned with the effects of application in the hospital area of "disinfectants", a term which, according to Patterson's definition (1), is commonly used of substances applied to inanimate objects for the purpose of destroying disease germs or other harmful microorganisms (but not, ordinarily, bacterial spores).

Under the authority of this legislation certain testing methods have been adopted and promulgated which are designed to extend a measure of protection to the consuming public in the matter of both

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purchase and use of disinfectants, through regulatory supervision of their formulation and labeling. In contrast to this, many hospitals labor under confusing misinformation regarding the performance of the different categories of disinfectants, as well as their fitness for general or for special uses in the several relevant hospital activities, viz., medical, surgical, housekeeping and nursing; the apparent reason is that only a minimum of regulatory supervision is being applied in this area, no doubt, on the assumption that all hospital departments are staffed by experts, familiar with the correct types of disinfectants for their respective purposes, as well as with the proper use of the applicable types. However, a careful study of the situation reveals that such is not the case; actually the several varieties of so-called "expert" opinion in the hospital area vary all the way from the "no-disinfection" school at one extreme, to the direct application of disinfectant concentrates at the other, with inadequate types of disinfectants or improper procedures in between.

Yet the role of disinfection in the hospital is by no means an unimportant or an academic subject. There exists an enormous amount of literature on the subject of hospital infection (and cross-infection) of environmental origin, the several possible routes of its spread, and the different methods of its control, both demonstrable and presumptive, by means of proper disinfectant measures.

Staphylococcal Sepsis and Antibiotics

The problems of infection and cross-infection have been facing hospitals long before the appearance of antibiotic drugs (2). However, following their introduction and extensive use, the situation became unexpectedly worse, owing to the gradual emergence and increasing dissemination of bacterial strains resistant to the action of antibiotics. Hospitals and surgeons who have come to rely upon antibiotics as prophylactic weapons against infection, now recognize the breakdown in the offensive as well as in the defensive effectiveness of these drugs (3). As Lowbury (4) expressed it succinctly in a recent comprehensive review: "The dilemma of hospital infection has been complicated rather than solved by chemotherapy".

The essential difference between the situations existing in the pre-antibiotic and the antibiotic periods, is that in the former period hemolytic streptococci were most often involved, while in the current antibiotic era the staphylococcal complications are in the ascendency,

as shown in numerous recent papers published in this country and abroad (5-24).

Environmental contamination with, and aerial dissemination of staphylococci in the hospital area are of primary relevance to post-operative wound infection, also to staphylococcal pyodermas on wards as well as in nurseries. Among the other manifestations of the same basic phenomenon are staphylococcal pneumonia, enterocolitis and parotitis.

This is not to say that infection by hemolytic streptococci has ceased to be a problem altogether; on the contrary, as reported by Gibson and Colman (19), and most recently by Rountree (20), it is precisely the antibiotic-resistant staphylococcus which, acting as the primary invader, facilitates streptococcal colonization of the surgical wound, in spite of a preceding prophylactic parenteral administration of penicillin. (What happens here is that the antibiotic-resistant staphylococcus, being a powerful producer of penicillinase, literally prepares the field for the invasion and infection by streptococci, even though the latter may belong to a penicillin-sensitive strain) (21).

Although it seemed, at first, that penicillin-resistant staphylococci might be controlled by other antibiotics, a recent report by Spink (22) points to the isolation in a major hospital of numerous coagulase positive strains, resistant to streptomycin, chloramphenicol, tetracycline (also oxy- and chlortetracycline) and erythromycin. While some newer antibiotics (oleandomycin, vancomycin) are being credited with the capacity of controlling staphylococci resistant to other antibiotics, only time will tell whether or not new resistant staphylococcal mutants will develop, once these new antibiotics come into general use.

Parenthetically speaking, the hospital problem posed by staphylococcal sepsis illustrates strikingly the fallacy implied in the older "phenol coefficient" requirements based upon the test results with only one microorganism, viz., *S. typhosa* which, moroever, is usually unrepresentative of the type of bacteria against which remedial measures should be taken. Nevertheless, numerous hospitals, as well as state health agencies and other authorities continue to base their evaluation of hospital disinfectants exclusively upon the phenol coefficient figure alone, evidently in ignorance of the fact that the *S. typhosa* phenol coefficient may conceal a practically complete lack of capacity for action upon staphylococci (also upon other important pathogens) (27).

Rationale of Disinfection Routine

Thus, there appears to have arisen a need for a change in those hospital procedures where the vicious cycle of environmental contamination and infection has established itself. As to the role of staphylococci in this picture, it has been known for some time that the infective agent may become air-borne in the form of dried fomites after originating in a septic wound, and that one of its primary means of distribution is the upper respiratory tract of the hospital personnel. However, at one stage of this cycle, the pathogens sediment on floors, furniture and blankets whence they are redispersed into the air to settle on a clean surgical wound, or to infect patients confined to bed, etc. According to a distinguished authority, "The floor is the big reservoir for sepsis in the hospital"; nevertheless, it is "inadequately cared for in most institutions" (17). Fig. 1 illustrates the pathways of infection by staphylococci, according to Rountree (20).

While this is not the place for a listing of all the measures required to eliminate the risk of air-borne transmission of infection, one must assume that the fundamental importance of the several

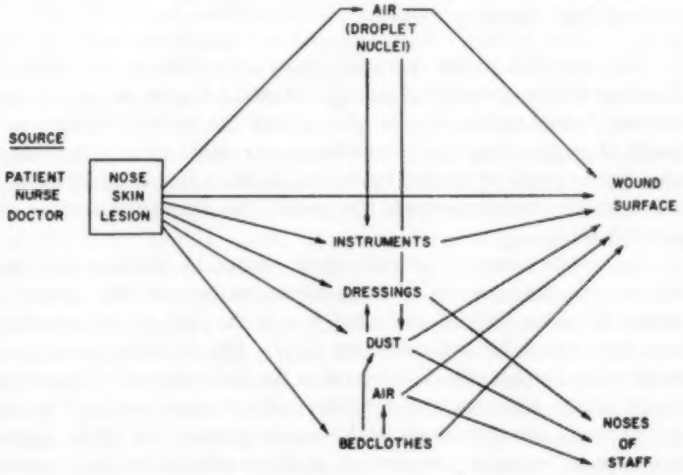

FIGURE 1.
SOURCES OF STAPHYLOCOCCI AND PATHWAYS OF WOUND INFECTION
(ROUNTREE)

aspects of correct aseptic technique is fully appreciated by those concerned, i.e., with respect to the sterilization or disinfection of instruments and appliances, the correct preparation of the patient, proper dressing technique, maximum attention to cleanliness of the hands of the personnel, etc. However, as environmental sanitation appears to play so important a role in this picture, some relevant comment may be justified.

Since staphylococci are thought to be most directly implicated in creating the problem of post-operative sepsis, an ultimate control of the inciting condition is not likely to be achieved until the hospital personnel involved is made to be aware of the following facts:

1. "Soap-and-water" cleaning does not go far enough because it cannot be relied upon to kill staphylococci (25).

2. Environmental disinfection calls for the use of a product which is demonstrably germicidal for staphylococci (in addition to other pathogens which are potential spreaders of hospital infection).

3. The operating room and connecting floor areas must be disinfected daily, i.e., by thorough mopping with a germicidal solution, following clean-up.

But attention to the operating room area alone is not sufficient. Mopping with a germicidal solution should be part of regular and frequent housekeeping routine throughout the entire hospital, as a means of suppressing the "secondary reservoirs" from which infectious matter could be carried by drafts, on shoes and in other ways, to and from the recovery room, the wards, the maternity section, the nursery, etc.

As to the dispersal of pathogenic matter by blankets and bedclothes, one hears again of suggestions to control this source of fomites by oiling, in spite of the fact that in the past, oiling procedures have been found distinctly wanting (26). On the other hand, using an effective, non-volatile disinfectant in the final rinse after laundering should permit retention of a sufficiency of the active principle to control bacterial contamination, and thus to protect the fabric against becoming a "secondary reservoir" of dispersible infectious particles.

What are the supplementary requirements of a disinfectant for the purpose in question, i.e., over and above the axiomatic requirement of non-specific, antimicrobial action?

Obviously, routine disinfection even when performed with frequent regularity, cannot be expected to yield the desired result if the character of the disinfectant is such as to permit reinfection of the treated surface soon after disinfection. Thus, while a given disinfectant may produce a germicidal effect at the time of its application, this effect may be but temporary in character, except where the disinfected area acquires and retains a more enduring antibacterial potential, i.e., the capacity for inactivating infectious matter settling upon it during the period between the individual applications of the disinfecting process. The factors in the dissipation of the antibacterial potential, following inadequate disinfection, may be physical or chemical or both, depending upon the character of the disinfectant used, and of the surfaces or objects treated. In any case, the application of a disinfectant devoid of prolonged residual action should not be expected to oppose the establishment of "secondary reservoirs" of pathogenic bacteria, including the troublesome staphylococci which may remain viable for several weeks after dispersal by a patient or a carrier (14).

Staphylococcal Contamination of the Air

The effect upon environmental air contamination of activity going on in an operating theater has been studied by Blowers *et al.* (9). It should be stressed that the highly unsatisfactory condition found by these investigators was not due to any single factor acting in the operating theater area alone, and that it was remedied only upon the institution of extensive reforms, both structural and procedural, throughout the hospital. However, it is noteworthy that a direct relation has been established between the total bacterial count and the *Staphylococcus aureus* count, at the several stages at which air contamination was measured. This leads to the conclusion that control of the total bacterial contamination of the atmosphere is bound to reduce also the risk of staphylococcal contamination and infection.

The reason for dwelling upon this subject with some emphasis is that such a conclusion ties in with certain important findings made recently by Lester and Dunklin (28). In an extension of the results obtained originally by Klarmann, Wright and Shternov (29), these authors showed that the residual antibacterial capacity imparted to various test surfaces by treatment with a particular synthetic phenolic disinfectant,* remained in evidence with respect to dust-borne micro-

* Based on o-phenylphenol, and known as "O-syl".

organisms, as well as to spray-dried pathogens for several days or even weeks. More recently, Lester and Dunklin (30) found that as a result of regular application of this disinfectant to the floor of a recovery room and connecting entrance hall it was possible to reduce bacterial contamination by some 95 per cent, in spite of the daily use of the premises by physicians, nurses and attendants bringing in fresh contamination continuously. Equally, if not more significant, is the observation that simultaneously the bacterial count of the environmental air was depressed by 60 to 80 per cent, owing to the decontamination of the floor area.

Effect of Disinfectants on Antibiotic-Resistant Staphylococci

At this point, some reference should be made to the action of disinfectants upon antibiotic-resistant strains of staphylococci. Recently three such strains were subjected to a test in our laboratory using both the "official" A. O. A. C. "Phenol Coefficient" and the A. O. A. C. "Use-Dilution" techniques (31). In the following tables I and II, the coagulase-positive strain No. 138 is penicillin-resistant, while strains No. 879 and 889 exhibit a cross-resistance with respect to several antibiotics, viz., penicillin, streptomycin, aureomycin and neomycin; strain 889 is also resistant to erythromycin. Strain No. 209 is the standard strain of *M. pyogenes* var. *aureus* as specified for use in the two A. O. A. C. test procedures cited.*

The results given in tables I and II indicate that staphylococci which became resistant to the several antibiotics mentioned did not acquire any increased resistance either to phenol or to the three phenolic disinfectants studied; in one case (strain No. 889), the resistance to phenol as well as to the phenolic germicides appears to be distinctly lower than that of the standard strain No. 209 (Table II).

By combining these findings with those mentioned before, viz., the reduction of bacterial air contamination through the disinfection of surfaces, and the established relation of the staphylococcal to the total bacterial air count, one arrives at the conclusion that the maintenance upon the critical surface areas (floors, also furniture, shelves, etc.) of a persistent antibacterial potential should go far toward reducing the staphylococcal contamination of the enclosing air-spaces, thereby lessening the risk of air-borne infection by staphylococci.

* The three phenolic disinfectants listed in Tables I and II are known as "O-syl", "Amphyl" and "Lysol" respectively.

TABLE I

"USE-DILUTION" TESTS WITH ANTIBIOTIC-RESISTANT STAPHYLOCOCCI

Disinfectant by Type or Active Ingredients	Dilution	Staphylococcus Strain No.	Number of Rings Tested	Number of Rings Positive	Number of Rings Negative
Phenol U. S. P.	1:20	209	10	0	10
		138	10	0	10
		879	10	0	10
		889	10	0	10
o-Phenylphenol (p.c. 5)	1:100	209	50	1	49
		138	40	2	38
		879	40	1	39
		889	40	0	40
o-Phenylphenol and *p-tert.* amyl. phenol (p.c. 10)	1:200	209	50	1	49
		138	40	0	40
		879	40	2	38
		889	40	0	40
o-Phenylphenol and cresylic acid (p.c. 5)	1:100	209	50	1	49
		138	40	2	38
		879	40	2	38
		889	40	0	40

Concluding Remarks

The problem of controlling hospital infection in general, and of staphylococcal sepsis in particular, has become seriously aggravated by the emergence of antibiotic-resistant strains of staphylococci; its solution concerns the several relevant areas of hospital activity, viz., medical, surgical, housekeeping and nursing. All of these activities require a searching bacteriological scrutiny at frequent intervals in order to eliminate the risk of interference by bacterial contamination, actual or suspected, personal or environmental.

There exists persuasive indicative evidence in support of the proposition that regular concurrent disinfection with the proper type of germicide represents an important measure directed against bacterial, and especially against staphylococcal contamination of the environment. To satisfy the pertinent requirements, it is held that

the disinfectant employed should be irreversibly germicidal (rather than inhibitory), also non-selective in action against the several pathogens capable of causing or spreading nosocomial infection, including strains which have acquired a resistance to antibiotics. Moreover, it should be capable of imparting a prolonged antimicrobial potential to disinfected surfaces, characterized by their capacity to inactivate sedimenting pathogenic matter being disseminated by patients or personnel for some time after the disinfection of such surfaces.

While the "official" testing methods for disinfectants, notably the "Phenol Coefficient" and the "Use-Dilution" tests furnish important, if not definitive, means of evaluation of disinfectants promoted for use in hospitals, it is held that more supervisory attention to this matter should be devoted on the proper regulatory level in order to make sure that the hospitals employ the correct types of products which are

TABLE II

"PHENOL COEFFICIENT" TESTS WITH ANTIBIOTIC-RESISTANT STAPHYLOCOCCI

Disinfectant by Type or Active Ingredients	Staphylococcus Strain No.	Minimum Concentrations Germicidal in Minutes		
		5	10	15
Phenol U. S. P.	209	1:60	1:60	1:70
	138	1:60	1:60	1:60
	879	1:60	1:60	1:70
	889	1:60	1:80	1:100
o-Phenylphenol	209	1:150	1:200	1:200
(p.c. 5)	138	1:160	1:180	1:200
	879	1:160	1:200	1:250
	889	1:250	1:400	1:450
o-Phenylphenol and	209	1:300	1:350	1:400
p-tert. amyl phenol	138	1:350	1:450	1:500
(p.c. 10)	879	1:400	1:500	1:600
	889	1:600	1:600	1:800
o-Phenylphenol and	209	1:160	1:200	1:250
cresylic acid	138	1:160	1:200	1:200
(p.c. 5)	879	1:160	1:200	1:250
	889	1:300	1:350	1:500

suited to their varied germicidal needs; this would call also for the early elaboration and promulgation of such additional bacteriological screening tests as would assure the use of materials possessed, at least, of a presumptive capacity to control microbial interference in the several areas of hospital activity.

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TRANQUILIZING DRUGS *

By G. Victor Rossi

DRUGS producing artificial psychoses are not new—neither are tranquilizing agents wholly novel—but their relationships to neurochemistry and mental disorders have only recently excited the imagination of the research worker and the clinician alike.

The effects of certain chemical substances on mood and personality changes have long been appreciated, but attempts to explain their mechanism of action as a rational basis for their therapeutic usefulness are in their incipiency. Independent lines of study are being pursued in an effort to arrive at a "biochemical correlation with personality"—but regardless of the fact that it runs countercurrent with due scientific process and our natural desire to "pigeon hole" drugs into discrete categories of action and reaction—no single thread has yet emerged to tie the dozen or so "ataraxics" now available into a digestible and unified concept.

At our present state of knowledge, I believe that we should cite only two drugs as having firmly established ataractic properties—these are reserpine (Serpasil) and chlorpromazine (Thorazine). It is highly probable that the very close chemical relative of reserpine, rescinnamine (Moderil), which differs from reserpine only in that cinnamic acid replaces benzoic acid, will prove to share the characteristic actions. This is also true of promazine (Sparine), which differs from chlorpromazine only in that it lacks a chlorine group at the phenothiazine nucleus.

An increasing amount of evidence supports the premise that these ataraxics affect the central nervous system, particularly the activity of the reticular system, in a manner fundamentally different from the barbiturates, to produce calmness, tranquility and amelioration of tension without excessive drowsiness or deleterious effect on mental performance.

Meanwhile the burden of proof falls upon the galaxy of extensively promoted products that remain before they can be validly designated as ataraxics rather than non-specific sedatives or agents blocking polysynaptic neural transmission, found to be effective in various forms of excessive muscular tension.

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* Presented before the Physicians and Surgeons of the Pennsylvania Railroad, Atlantic City, N. J., October 13, 1956.

Let us then unravel a few promising threads from the loose pattern spun of "mental health drugs", to find only that many lead again to knotted ends.

Turning back the pages of time, we find that for centuries the dried tops of the Peyote cactus, which grows extensively in the Rio Grande region of the United States and Mexico, have been ingested by certain American Indian Tribes during sacramental ceremonies in the belief that the Holy Spirit resided in the Peyote. Mescaline, the active principle of Peyote, produces definite anxiety and vivid hallucinations generally manifested as distortions of color and space perception.

In a similar fashion, plant preparations containing bufotenine were used by primitive man, including South American Indians and the early Vikings, to produce temporary ecstatic states of depersonalization and hallucinations.

To cite another parallel situation—it has also been known for centuries that the mind is affected by eating bread made from grain infested with ergot fungus. Indeed, epidemics of ergotism have driven entire populations mad in parts of Europe and Russia.

These isolated medical curiosities were channeled into a pattern which set the stage for today's tranquilizers. In the mid 1940's Hoffman, a chemist, discovered that temporary mental changes could be induced by microgram quantities of the newly synthesized lysergic acid diethylamide (commonly abbreviated LSD from the German, lyserg saure diathlyamide), which is the basic structural nucleus of the active ergot alkaloids. As a result of accidental absorption he experienced peculiar restlessness and dizziness—"a not unpleasant state of drunkenness, characterized by extremely stimulating fantasy, associated with an intense kaleidoscopic play of colors".

A search for a common denominator among these chemicals (mescaline, bufotenine, ergot, LSD and others with similar properties), which collectively are known as the hallucinogens or psychomimetics, revealed the presence of an indole nucleus or an indole-like structure.

Normal persons under the influence of these substances can describe exactly what they are experiencing without losing awareness of the fact that they are under the influence of the drug. Thus, unlike the schizophrenic, "the thread of reality is not cut".

On this basis, the Canadian investigators Hoffer, Osmond and Smithies postulated that the discovery of compound(s) occurring in

the body with an indole-like structure would provide a vital clue to the etiologic factor in schizophrenia. Two such substances were offered as candidates to support this hypothesis: adrenochrome and serotonin.

Many clinicians have noted the transient psychological disturbances which occasionally follow the injection of adrenalin, especially if the adrenalin solution is somewhat deteriorated, oxidized or shows a pink discoloration—indicating the presence of adrenochrome.

Adrenochrome injected in human volunteers produced psychoses similar to those elicited by other hallucinogens, notably mescaline and LSD. Thus it was postulated that some abnormality of adrenalin metabolism might result in excessive adrenochrome accumulation in the body, which would be responsible for mental aberration. As these early experiments have never been fully confirmed, this hypothesis remains equivocal.

The second candidate, a substance which occurs naturally in the body and displays the indole nucleus is 5-hydroxytryptamine—a metabolic oxidation product of the essential amino acid tryptophane. This compound was isolated from the enterochromaffin system and termed enteramine by Erspamer of Italy. In this country, Page characterized the substance as identical to a vasoconstrictor factor liberated from blood platelets and applied the term serotonin, which is the empirical designation most frequently employed. Serotonin is believed to be an important neurohumoral transmitter in the central nervous system, functioning in a manner similar to acetylcholine. The hallucinogen LSD has been demonstrated to be a serotonin antimetabolite, capable of at least partially antagonizing the central and peripheral actions of this neurohormone. The deficiency of serotonin in the brain induced by LSD, most likely due to reduced serotonin synthesis, has been considered as a possible cause of the hallucinations observed following administration of LSD, and it was further suggested that some of the naturally occuring mental disorders might similarly arise from a lack of serotonin in the brain. Indeed, Gaddum has termed serotonin as the substance which "keeps us sane".

A considerable body of evidence has accumulated indicating that the tranquilizing effects of reserpine are mediated through the release of serotonin in the brain: (1) Reserpine and serotonin share central and peripheral effects which are blocked by LSD. (2) Reserpine releases serotonin from its binding sites in various body tissues including the brain. (3) Only pharmacologically active Rauwolfia

alkaloids possess the ability to release serotonin, whereas the commonly employed sedatives, hypnotics and narcotic analgesics do not. (4) Reserpine is no longer detectable in the brain a few hours after its administration, but the pharmacologic effects, which persist for about two days, parallel the duration of depression of serotonin concentration.

However, several discrepancies have recently been noted which argue against complete acceptance of serotonin release as the major mechanism of reserpine-induced tranquilization. For example, serotonin is present only in extremely low concentrations in the brain, whereas large amounts of exogenous serotonin are required to elicit significant pharmacologic effects. Even the administration of large doses of serotonin to schizophrenic patients has been of little or no benefit. This may, of course, be related to inadequate transport across the blood brain barrier. In addition, the 2-bromo derivative of LSD, like the parent molecule, is a potent serotonin antagonist but does not share the characteristic hallucinogenic activity of LSD. This further indicates that disturbances in serotonin metabolism may only be coincidentally involved in the mental changes produced by ataractic and psychomimetic drugs. The present consensus favors serotonin release by reserpine to be responsible for certain side effects associated with the administration of reserpine, such as conjunctival and nasal congestion, increased gastrointestinal motility and possibly hypersecretion.

This brings to mind a parallel in the case of d-tubocurarine, which exerts its typical skeletal muscle relaxing effect by preventing repolarization at the myoneural junction and coincidentally releases histamine from its binding sites in the body. No one today accepts histamine release as the mechanism responsible for the characteristic action of curare, although it is blamed for the undesired hypotension and bronchospasm commonly associated with curare administration. However, the concept of serotonin release, although no longer fully tenable, has performed an invaluable service to medicine by directing attention to the possible role of biochemical lesions in mental disorders and the hope of discovering specific therapeutic agents to correct the abnormality.

The aphorism aptly stated by Himwich, "experience has taught us that drugs have multiple sites of action, each with different thresholds of excitability," certainly applies to the heterogenous group of chemicals dubbed tranquilizers. Although the sites and mechanism

of action of these drugs remain to be elucidated, considerable progress has already been made in this direction.

Clinicians have noted the striking similarity between states of parasympathetic predominance and the syndrome elicited by reserpine, including: sedation, miosis, hypothermia, hypotension, bradycardia, gastrointestinal hypermotility and hypersecretion. Many of these effects are also characteristic of chlorpromazine. The consensus in regard to both reserpine and chlorpromazine is that these symptoms are evidence of inhibition of the sympathetic representation in the posterior hypothalamus.

The facilitation of synaptic transmission observed with reserpine led Schneider to postulate that depression of hypothalamic activity by reserpine, and possibly chlorpromazine, is largely an expression of increased cortical inhibition. Unlike the barbiturates, both reserpine and chlorpromazine provide tranquilization without hypnosis or the typical EEG changes characteristic of sleep. Himwich and Rinaldi attribute this to stimulation of the mesodiencephalic activating system (MDAS), an area depressed by barbiturates. Thus, reserpine or chlorpromazine sedation, mediated by hypothalamic inhibition, is tempered by the arousal reaction evoked by stimulation of the activating system. An unfortunate side reaction resulting from the effect of these drugs on the activating system is the production of Parkinsonism, a complication not uncommonly observed with large doses of either reserpine or chlorpromazine. Recent electroencephalographic studies demonstrate that after administration of chlorpromazine the amygdaloid nuclear complex consistently shows increased spontaneous activity, not observed following administration of barbiturates.

It is apparent from this brief survey that the therapist has been endowed with a new class of psychopharmacologic agent, the ataraxic or tranquilizer, which differs fundamentally from the traditional sedative in action and usefulness. However, we reiterate that much basic investigation lies ahead before many of the recently marketed aspirants to this title can justifiably claim advantage over the sedative and muscle relaxant drugs familiar to more than a generation of physicians. While a considerable measure of success has already been achieved with the tranquilizing agents now at hand, the hope of medicine is predicated on the belief that improved versions of these molecules will soon be available. Indeed, the most lasting contribution of the current interest in hallucinogens and ataraxics may well be the impetus provided to resolve the biochemical answers to abnormal behavior.

APPENDIX

Ataraxics

Rauwolfia alkaloids
- Reserpine (Serpasil, Ciba)
- Rescinnamine (Moderil, Pfizer)

Phenothiazine derivatives
- Chlorpromazine (Thorazine, S. K. & F.)
- Promazine (Sparine, Wyeth)
- Proclorperazine (Compazine, S. K. & F.)
- Promethazine * (Phenergan, Wyeth)

Others
- 2-ethylcrotonylurea (Nostyn, Ames)
- Dioxolane (Dimethylane, National)
- Meprobamate (Equanil, Wyeth; Miltown, Wallace)
- Hyroxyzine (Atarax, Roerig)
- Benactyzine (Suavitil, Glaxo)
- Azacyclonol (Frenquel, Merrell)

Muscle Relaxants

Mephenesin (Lissephen, Abott; Tolserol, Squibb)
Diethyl propanediol (Prenderol, Squibb)
Meprobamate ** (Equanil, Wyeth; Miltown, Wallace)
Zoxazolamine (Flexin, McNeil)

Cerebral Stimulants (Euphoriants, "Antidepressants")

Pipradol (Meratran, Merrell)
Methyl-phenidylacetate (Ritalin, Ciba)
Amphetamine derivatives

Newer Non-barbiturate Sedative-Hypnotics

Methylparafynol (Dormison, Schering)
Ethchlorvynol (Placidyl, Abbott)
Ethinamate (Valmid, Lilly)
Methyprylon (Noludar, Hoffman-LaRoche)
Glutethimide (Doriden, Ciba)

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* Most widely known for its antihistaminic activity.
** Also claimed to have ataractic properties.

DRUG INFORMATION SOURCES *

(France, Switzerland, Austria)

FRANCE

La Nouvelle Officine; Répertoire Général de Pharmacie Pratique (Dorvault). Paris, Vigot Frères, 1955. 2 v. (1104, 1812 pp.) Approx. $40.00.

A comprehensive reference work covering the entire field of pharmacy and pharmaceuticals. Part 5, Dispensaire pharmaceutique, comprises all of Volume 2. Monographs are entered alphabetically, usually under generic name of drug; in some instances drugs are grouped in broad classes, as in the case of antibiotics, arsenicals and organotherapy. Monographs report alternate names from all countries, including some proprietary names (but not manufacturers), composition, description, assay methods, indications and dosages. Two alphabetic indexes to this section are included, one for generic, proprietary and chemical names, and the other for the extensive compilation of foreign names (e.g., synonyms located in the pharmacopeias and dispensatories of other countries). Publisher's address: 23, rue de l'École-de-Medicine, Paris 6e.

Dictionnaire de Spécialités Pharmaceutiques, edited by Louis Vidal. Paris, Office de Vulgarisation Pharmaceutique, 1956. Four separately paged sections, approx. 2400 pp. 1400 francs.

Section 3 is an extensive alphabetic list of specialties which reports for each drug its manufacturer, composition, action, indications, dosage and supply. The other sections are a therapeutic index, a list of common and chemical names for specialty drugs (reprinted from *Therapie* 10:97-159 (1955)), and a list of manufacturers with their products. A new edition appears annually. Publisher's address: 11, rue Quentin-Bauchart, Paris 8e. [The 1957 edition, at 1600 francs, has been announced.]

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* A World List; compiled by the Pharmaceutical Section, Science-Technology Division, Special Libraries Association.

Le Livre Blanc; Formulaire Médical, 1955. Paris, Editions Henri Perrier, 1955. 1996 pp.

Section 2 is a compilation of important drug products marketed in France with detailed information about the manufacturer, composition, actions, indications, dosage and how supplied. Drugs are listed alphabetically under proprietary names. Section 3 is a list of manufacturers with products as covered in Section 2. A detailed therapeutic guide to products and their dosages as used in specific diseases, an alphabetic list of all products of French firms with references to their manufacturers and an alphabetic list of all manufacturers with their addresses complete the volume. Revised biennially. Publisher's address: 3, rue Aubriot, Paris 4e.

Formulaire des Médicaments Nouveau. 40th ed., edited by René Weitz and Jacques Singier. Paris, Librairie J. B. Baillière et Fils, 1953. 384 pp.

Monographs are entered alphabetically by name of drug (usually generic or chemical) and report synonyms (including proprietary names and experimental numbers), chemical formula, preparation, description, therapeutic properties, uses and dosage. Monographs are full and descriptive and contain historical material and literature references. A few monographs on broad classes of drugs are included. Manufacturers' names are not reported. A separate alphabetic list of synonyms cross references proprietary, generic and chemical names. Publisher's address: 19, rue Hautefeuille, Paris 6e.

Formulaire Médical de l'Union Française. Paris, La Thérapeutique dans le Monde, 1955. 618 pp.

A physician's handbook of drugs arranged in the following sections: I, List of pharmaceutical manufacturers and their specialties; II, Therapeutic index; III, Alphabetic list of pharmaceutical products with information about composition, actions, indications, method of administration, dosage, how supplied and manufacturer; IV, Practical information including dosage tables, diets, biological constants, prophylaxis of contagious diseases, antidotes, etc.; V, Lists of official health services of Paris and of the Medical Corps of the Union Française. Publisher's address: 111 rue de l'Universite, Paris 7e.

Le Livre du Praticien; Guide Thérapeutique. 6th ed., 1952-1953 edited by A. -L. Clairville. Paris, SIPUCO, 1952. 675 pp.

A physician's handbook of drugs and therapy arranged in the following sections: I, A selection of literature references on drugs; II, Lists of synonyms, experimental compounds, foreign drugs with their French equivalents; III, Therapeutic index; IV, Systematic pharmacy; V, Short list of pharmaceutical specialties with information about composition, actions, indications, and how supplied. There is also a list of manufacturers with their addresses. A comprehensive alphabetic index is included. Publisher's address: 35, rue des Petits-Champs, Paris 1e. [No answer received at publication time to request for information about new edition.]

Formulaire de Poche du Médecin-Praticien Suivi d'un Memento Thérapeutic avec Indications des Méthodes Nouvelles de Traitement. By E. Agasse-Lafont. Paris, Vigot Frères, 1953. 727 pp.

A physician's handbook based on the *Codex Français*. Entries are arranged alphabetically by common name of drug or sometimes broad classes of drugs. They report preparation, properties, actions, uses, dosage, maximum dosage, toxicity tables, formulas for combinations and names of specialties in which the individual drug is used. Manufacturers are not listed except when included in drug name. An alphabetic therapeutic index is included. The alphabetic general index covers both drug names and therapeutic indications. A supplement, *Les medications nouvelles de 1949 a 1952,* brings coverage up-to-date in accordance with the *Codex* Supplement 1953. Publisher's address: 23, rue de l'Ecole de Medecine, Paris 6e.

SWITZERLAND

Repertorium Pharmazeutischer Spezialpraparate, Sera und Impstoffe, edited by Herbert Ludwig with the collaboration of L. V. Furland and E. Loeliger. 1st ed. Basel, Verlagsgesellschaft Beobachter, 1946. 1308 pp. Sw. Fr. 62.-, 26.-, 32.-.

The principal portion of the *Repertorium* is an alphabetical list of specialties, sera and vaccines, with information about manufac-

turer, composition, indications, how supplied, dosage, obligations of dispensing, permission to sick-clubs, year of introduction and, in some instances, literature references. A table of indications and a list of manufacturers with their products are also included. The text is in German, but the production of German, French, Italian, Spanish, Swiss, Swedish, Norwegian, Dutch, Belgian, Danish, Czech, Hungarian, British and American firms is covered. Supplements 1 (1947) and 2 (1950) contain new material and supplementary references to preparations in the original list. According to the publisher, the *Repertorium* is not to be revised. Publisher's address: Lautengartenstrasse 23, Basel.

Mitteilungen über Neue Pharmazeutische Spezialpraparate/ Aperçu de Spécialités Pharmaceutiques Nouvelles. Bern, Documentation Galenica Bern. Cards 4⅛" x 5 13/16".

In this card service on pharmaceutical specialties, products are entered by proprietary name, one product to a card. For each product is given manufacturer, composition (sometimes with chemical formula), actions, indications, contraindications, dosage, supply and sometimes literature references. The service is very prompt and, like the *Repertorium* (see preceding entry), covers important drugs of all countries. The text may be in French or German.

Übersicht der Gebräuchlichen und Neueren Arzneimittel für Ärzte, Apotheker und Zahnärzte. By E. Bernoulli and H. Lehmann. 8th ed. Basel, Benno Schwabe & Co., 1955. 508 pp. Approx. $4.50.

A handbook of remedies, classified according to body regions and pharmacologic effects. Reports on individual drugs are entered under generic names. The general discussion either on individual drugs or on classes of drugs covers composition, properties, actions, indications, contraindications, method of administration, dosage and maximum dosages. A list of individual drug specialties and combinations follows the general discussion. Additional features include a list of representative formulas for drug combinations, a table of maximum doses, a list of contrast media and a therapeutic index. A general alphabetic index lists all drug names.

Répertoire Alphabétique des Marques Internationales. Volume 1/2, classes 1-5. Zurich, A. W. Metz & C. A. Geiger, Agents de Marques, 1925 to date.

Volume 1/2 of this list of international trade marks covers classes 1-5; class 5 is pharmaceutical products. Proprietary names of all countries participating in the "Madrid arrangement" of the International Bureau at Berne are listed alphabetically with other trade marks [U. S. not a participant]. New marks and modifications are listed annually; cumulations were published for 1946-1949 and 1950-1953 and a reprint covering 1933-1945 was issued in 1954. Class number, registration number, registrant and reference to the nature of the modification are tabulated in the current volumes. Annual volumes are priced at Sw. Fr. 40.- and cumulations st Sw. Fr. 65.- and 75.- (1946-1949). Publisher's address: Pelikanplatz 15, Zurich 1.

Catalogue de la Société Pour la Reglementation en Suisse de Produits Pharmaceutiques et Hygiéniques Spécialisés par des Marques Déposées. Geneva, Siège de la Société, 1956. 333 pp.

This alphabetic price list of trade-name drugs marketed in Switzerland is published every year on June 15th. It includes names of manufacturers and all dosage forms with prices to public, physician and retailer. A brief summary of the regulatory policies of the Society precedes the list.

Monatsbericht der Interkantonalen Kontrollstelle für Heilmittel. Bern, The Kontrollstelle. Current.

This monthly listing of new drugs registered by the Kontrollstelle reports of manufacturer, brief statement of composition, indications, how supplied and price.

AUSTRIA

Austria-Codex, compiled by Otto Zekert. Vienna, Österreichisher Apotheker-Verlag, 1955. 756 pp.

Part 2 is an alphabetic list of specialties registered for sale in Austria; individual entries report briefly the name of the manufacturer, composition, indications, how supplied, price and dispensing

regulations. Biologicals, dietetic products and disinfectants are listed separately. Other sections are a therapeutic (actions and indications) index and a list of Austrian manufacturers and Austrian representatives of foreign manufacturers with their products.

Österreichisches Spezialitätenverzeichnis. Vienna, Hauptverband der Österreichischen Sozialversicherungstrager, 1955.

In separate lists (one for drugs available free through the state-controlled organization and one for drugs available by purchase) drugs are classified in numbered sections by pharmacologic action; both specialties and non-specialty drugs are included. For each drug information includes how it is supplied and price. An alphabetic list refers from drug name to the numbered sections in which information will be found.

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A limited number of reprints are available for distribution by the Committee at 30¢ each. Requests should be sent to the Chairman at the Library, Squibb Institute for Medical Research, New Brunswick, N. J. Payment should accompany order.

Regular distribution will not be undertaken by the Section. Individuals and libraries wishing to ensure continued receipt of "Drug Information Sources" may do so by entering subscriptions to *American Journal of Pharmacy*.

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A NOTE ON THE SOLUBILITY OF SODIUM BROMIDE IN HYDRO-ALCOHOL SOLUTIONS *

By Walter J. Ludwig and Martin Barr

SODIUM bromide is frequently used as an ingredient in liquid preparations containing alcohol in various concentrations. Since the solubility of this salt is not as great in alcohol as it is in water, it was deemed advisable to determine the solubility of sodium bromide in hydroalcoholic solutions of different strengths. Such solubility data can be used advantageously in the preparation of liquid pharmaceuticals.

Hydroalcoholic solutions of various concentrations were prepared and the exact strengths of these solutions in terms of per cent alcohol [1] were established using specific gravity values as determined by the pycnometer method (1). Sodium bromide, U. S. P. XV [2] was used throughout this study.

For the preparation of the experimental solutions, a quantity of four-ounce tincture bottles were thoroughly cleansed and dried. A quantity of rubber stoppers were boiled in a sodium hydroxide solution to remove any impurities and then thoroughly rinsed with purified water. An excess of sodium bromide was then added to 100 ml. of the individual hydroalcoholic solutions contained in the tincture bottles. The bottles were tightly stoppered and shaken, and were then placed in a reel with a capacity of 12 bottles, which was immersed in a constant temperature bath and rotated by a chain drive from a small gearhead motor at 25° for forty-eight hours. The mixtures were then filtered and the clear, saturated solutions were collected in four-ounce prescription bottles.

For the purpose of analysis, 10 ml. of each saturated solution were pipetted into a 250 ml. volumetric flask and made up to volume with purified water. A 25 ml. aliquot of each dilution was then assayed for sodium bromide content using the official U. S. P. XV

* From the Department of Pharmacy, Philadelphia College of Pharmacy and Science.

1. Throughout this paper the term "per cent alcohol" indicates per cent C_2H_5OH by volume.

2. Merck and Co., Inc., Rahway, N. J.

assay (2). The solubilities of sodium bromide in the hydroalcoholic solutions, in terms of the grams of salt dissolved in 100 ml. of the saturated solutions (% w/v) were calculated and are expressed in Table I and Figure I.

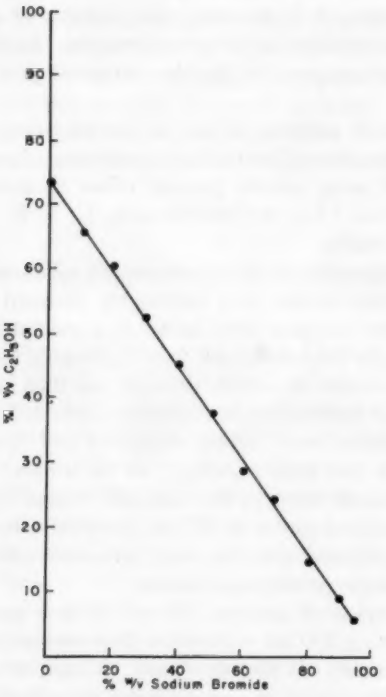

FIGURE I.

SOLUBILITY OF SODIUM BROMIDE IN HYDROALCOHOLIC SOLUTIONS.

TABLE I

THE SOLUBILITY OF SODIUM BROMIDE IN HYDROALCOHOLIC SOLUTIONS

% C_2H_5OH v/v in Solvent	Solubility Sodium Bromide % w/v
0.00	73.15
10.71	65.52
19.87	60.43
30.06	52.46
42.02	45.36
51.45	37.50
61.17	28.84
71.64	24.10
81.30	14.75
90.25	9.01
95.30	5.80

REFERENCES

(1) "United States Pharmacopeia," 15th Revision, Mack Publishing Co., Easton, Pa., 1955, p. 1141.

(2) *Ibid.*, pp. 642-643.

SELECTED ABSTRACTS

The Management of Pulmonary Tuberculosis. Tempel, C. W., and Wier, J. A. *U. S. A. F. Med. J. 8*:14 (1957). The authors reviewed the trends in the management of pulmonary tuberculosis. They pointed out that reversible lesions usually respond well to long term drug therapy with combinations of streptomycin sulfate and para-aminosalicylic acid, streptomycin sulfate and isoniazid, or isoniazid and para-aminosalicylic acid. However, there is a rather large group of patients who are improved by drug therapy but who never fully recover because of persistent cavitary residuals. In many of these cases, surgery could remove the focus of infection. However, in others surgery is not possible, for varied reasons. In the latter cases, the method of treatment to employ has been one of the most controversial problems.

Many patients without extensive cavitation but who have residual necrotic foci of infection recover and remain well. However, the threat of relapse under physical stress is ever present. The healing of such foci of infection is by the slow process of fibrous encapsulation and gradual drying out of the contents, which may require many years. It is known that present-day antimicrobial agents do not penetrate and sterilize these necrotic foci of infection. If the necrotic lesion sloughs instead of encapsulates, it may slough cleanly and heal completely, it may close over and form a tuberculoma, or it may slough and remain open with small pockets of necrotic tissue remaining in the cavity walls. In the latter two conditions, the danger of relapse remains present and, with the open lesions, the danger of communicability of the disease is also present. Further drug therapy under such circumstances may be of no value.

The authors pointed out the importance of rehabilitation of the tubercular patient. They reported that 84 per cent of 1,117 patients among military personnel were treated to the inactive stage of the disease in the hospital to which they were attached. These patients were then rehabilitated in a type of duty in which they had a reasonable chance of remaining well. Only 3.2 per cent of these patients relapsed during a five-year period.

A Comparison of the Oral and Intramuscular Administration of Penicillin. Henry, L., White, G., and Meynell, M. J. *Brit. Med. J.* No. 5009:17 (1957). Oral and intramuscular doses of penicillin were administered to six subjects. Their blood levels and 24-hour urinary excretion levels of the antibiotic were determined. A dose of 200,000 units each of phenoxymethyl penicillin and benzathine penicillin were given orally and crystalline penicillin G and procaine penicillin intramuscularly. Each of these four forms of penicillin were given in series to each of the six subjects. Each subject, therefore, served as his own control.

The intramuscular penicillin produced high blood levels which lasted for about 3 hours following crystalline penicillin G and about 6 hours following procaine penicillin administration. In both cases about 75 per cent of the biological activity of the antibiotic was recovered in the urine.

Following the oral administration of phenoxymethyl penicillin, the serum levels were lower than those obtained following parenteral therapy but were still adequate (0.1 unit per ml.) for a period of about 3 hours. However, the rate of absorption varied in some subjects. Only about 30 per cent of the ingested dose was recovered in the urine, reflecting the adverse effects of the intestinal tract upon the absorption of the penicillin. With benzathine penicillin the results were less satisfactory. Serum levels were usually not high enough for therapeutic effect and, if they did reach a level of 0.1 unit per ml., this level was not sustained for more than one hour. In addition, only between 5 and 10 per cent of the ingested dose was recovered in the urine.

The authors concluded, therefore, that oral penicillin was no substitute for parenteral penicillin when consistently high blood levels were required.

The authors also compared the results obtained with two test methods, the serial broth dilution method using *Staphylococcus aureus* and the plate method using *Sarcina lutea*. Both methods were used to determine serum levels of the antibiotics but only the latter for the urine levels because of the likelihood of contamination of the urine. They found that the plate method alone was suitable for absolute concentration level determination. Where only therapeutically minimum levels need be known, the tube method was satisfactory and was more simply performed.

The Use of Penicillin in the Treatment of Acute Sore Throat. Brumfitt, W., and Slater, J. D. H. *The Lancet* No. 6958:8 (1957). In practice, because of the difficulties and delay in obtaining bacteriological confirmation of a diagnosis of streptococcal sore throat, many cases are treated with antibiotics or with sulfonamides on the basis of clinical diagnosis alone. The authors found that it was difficult to distinguish the cases of streptococcal sore throat from non-streptococcal sore throat on the basis of symptoms. Therefore, they conducted a controlled study of the effect of penicillin on patients satisfying their symptomatic diagnosis whether or not streptococci were isolated from the throat of these patients.

Streptococci were isolated from the throat of 82 of 121 patients. To those patients assigned to receive penicillin, 300,000 units of procaine penicillin and 100,000 units of crystalline penicillin were given intramuscularly twice a day for 4 days. All patients were given aspirin gargles.

The authors found that the most striking effect of penicillin among the patients from whom streptococci had been isolated was the reduction in the duration of pyrexia and of leucocytosis. The duration of the sore throat was also shortened somewhat. There was not much reduction in edema and tissue injection, as compared with those patients receiving only symptomatic treatment. However, between the two non-streptococcal treatment groups, penicillin therapy did not significantly affect the course of the disease.

The authors concluded that intramuscular penicillin will only be useful in the treatment of cases of acute sore throat with pyrexia if hemolytic streptococci are present. The duration of symptoms will be reduced by about one day. No other beneficial effect can be expected, and the risk of inducing drug sensitivity must be given careful consideration.

The Treatment of Schizophrenia With Reserpine. Moore, J. N. P., and Martin, E. A. *Brit. Med. J.* No. 5009:8 (1957). The difficulty of the evaluation of the efficacy of a new treatment in psychiatry is well known. The authors evaluated the use of reserpine in the treatment of 119 cases of schizophrenia. Initially, treatment consisted of 2 to 8 mg. of reserpine orally each day. Later, the following regimen was used, 3 mg. orally throughout the course of treatment, 5 mg. intramuscularly the first evening, 10 mg. intra-

muscularly each evening for 3 to 7 weeks, reducing this to 5 mg. on alternate nights for 2 weeks, and finally 2.5 mg. on alternate nights before discontinuing injections. The side effects of this high dosage required modification of the dosage in some cases. However, the side effects sometimes relieved the patients by giving them physical ills to occupy them rather than mental ills.

Benefit was obtained in many cases of chronic schizophrenia where other types of treatment had failed to provide sustained remission. Untreated schizophrenia of insidious onset but without florid symptoms or gross personality deterioration may also respond favorably. Immediate results of reserpine therapy in acute schizophrenia was also impressive. In many of the cases in which improvement occurred, continued dosage with reserpine over prolonged periods of time seemed to be indicated.

Severe depression of the endogenous type with characteristic early morning waking and suicidal preoccupation was the most serious complication of the treatment. The incidence of this side effect was greatest in the schizo-affective type of psychosis. A past history of endogenous depression is a contraindication to the use of the drug.

An addendum indicating the results of a follow-up of most of the cases about a year after the initially assessment of results tended to verify the earlier conclusions. Only among the schizo-affective psychosis group had a minority maintained improvement.

Therapy for Improved Mental Function and Behavior of Elderly Patients. Katz, E. M., and Kowaliczko, Z. *International Record of Med. & Gen. Pract. Clin. 169:*596 (1956). A combination of factors designed to correct the relative cerebral anoxia and decreased rate of utilization of oxygen by the cerebral tissues characteristic of declining mental function in senility, was administered to 27 chronically ill male patients ranging in age from 52 to 86 years. The combination known as L-Glutavite, contained 3.48 Gm. monosodium L-glutamate, 45 mg. niacin, 0.6 mg. thiamine mononitrate, 0.8 mg. riboflavin, 30 mg. ascorbic acid, 11 mg. ferrous sulfate, and 910 mg. dicalcium phosphate. The above quantity of powder was administered 3 times a day for a period of 12 weeks.

Prior to treatment all of the patients suffered from various chronic illnesses as well as varying degrees of mental deterioration, apathy, fatigue, depression, lack of cooperation, and decreased motor activity. Following the course of treatment, 3 patients were classified as having shown excellent improvement, 9 were good, 6 were fair, and 9 showed little or no improvement. Thus, 67 per cent of the patients showed some degree of improvement in their mental and motor activity. The authors pointed out that those who failed to respond appreciably to this therapy were those with far advanced mental deterioration and severe physical disabilities. Where no serious incapacitating diseases existed, patients showed very encouraging improvement to treatment with L-Glutavite. The authors concluded that the factors in this preparation appear to be useful in the management of the elderly patient in whom apathy, fatigue, mental depression, anorexia and some decline in mental function are the principal symptoms.

BOOK NOTICES AND REVIEWS

Textbook of Pharmaceutical Compounding and Dispensing. Second Edition. Editors Rufus A. Lyman and Joseph B. Sprowls. xiv + 477 pages including index. J. B. Lippincott Co., Philadelphia, Pa., 1955. $9.75.

This is the Second Edition of the book first published in 1949 under the title, *Pharmaceutical Compounding and Dispensing,* and—as with the First Edition—the contributions of a number of pharmaceutical educators have been coordinated by the editors into a cohesive and well-arranged textbook. The subject matter is arranged in a logical sequence with the prescription and pharmaceutical Latin considered first and then followed by such chapters as Accuracy in Dispensing, Dosage Forms, Flavors, and Colors. Then come chapters on what might be best described as the application of chemical and physical-chemical principles to pharmacy followed by chapters on various liquid sysetems, semi-solids, etc. Incompatibilities of both inorganic and organic compounds are considered on a chemical basis. There are also chapters on such subjects as Dental Pharmacy and Hospital Pharmacy.

In preparing this Second Edition, the professional work involved in compounding and dispensing has been placed on an even better scientific foundation and the principles of physical pharmacy are drawn upon heavily in explaining the many phenomena that the student meets in his work. This is in line with modern trends in pharmaceutical education whereby the student is required to understand *why* a certain technique works or is required rather than just the simple fact that it is.

This modern textbook will undoubtedly be received even more enthusiastically than was its predecessor and the First Edition was widely accepted as a most useful textbook and reference for the student in dispensing pharmacy. The authors have done a fine job in preparing their copy and the approach which has been used is modern in every respect. Some of the older teachers in pharmacy may be critical of the rather liberal use of material which might be considered strictly in the fields of chemistry or physics. This, however, is distinctly the trend of modern pharmaceutical education and, if pharmacy is to grow in stature, it must be continued.

L. F. Tice

American Pharmacy. Fourth Edition. Editors Rufus A. Lyman and Joseph B. Sprowls. xvii + 478 pages including index. J. B. Lippincott Co., Philadelphia, Pa., 1955. $9.75.

This textbook is divided into two parts. Part I considers those subjects which for many years have been presented in the course titled Fundamental Principles and Processes of Pharmacy and deals with such subjects as Metrology, Specific Gravity, Heat, Purification and Clarification, Mechanical Subdivision of Drugs, Solutions, Colloids, Emulsions and Suspensions, Extraction, etc. While many schools have abandoned this type of course, many still offer it and, for those who do, this part of the Fourth Edition of *American Pharmacy* represents a very modern presentation of such material.

Part II of the book is concerned with pharmaceutical preparations and is presented for the beginning student in the laboratory work pertaining to pharmacy. This material follows the usual pattern, although it has been brought up to date in every respect even to the inclusion of a completely new chapter pertaining to radioactive pharmaceuticals.

The Fourth Edition of *American Pharmacy* appears to be a complete revision of its predecessors and to be up-to-date in every respect. It will undoubtedly continue to merit the extensive use as a textbook which the earlier editions enjoyed.

L. F. Tice

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